Ciências Farmacêuticas
X Congresso Iberoamericano
COIFFA CONFERENCIA IBEROAMERICANA DE FACULTADES DE FARMACIA A.C.

Impact of formulation of drug-containing blends on 3D printing by Fused Deposition Modelling

Ana I. Fernandes [a], Sara Figueiredo [b,c], Fátima G. Carvalho [c], João F. Pinto [b]

(a) Egas Moniz Center for Interdisciplinary Research (CiiEM); Egas Moniz School of Health & Science, Almada, Portugal
(b) iMed.ULisboa – Research Institute for Medicines, Faculdade de Farmácia, Universidade de Lisboa, Lisboa, Portugal
(c) LEF-Infosaúde, Laboratório de Estudos Farmacêuticos, Barcarena, Portugal

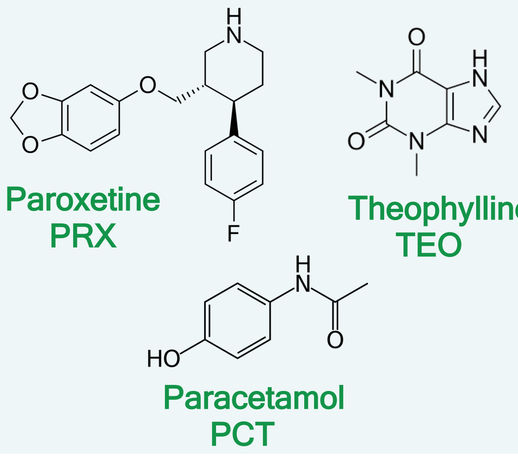
Introduction

- Fused Deposition Modelling (FDM) is paving the way for the digitally-enabled on-demand production of personalized medicines. The thermoplastic polymer matrix determines the mechanical and rheological properties of HME filaments (1), and ultimately the quality and performance of the 3D printed dosage forms (2).
- An inappropriate combination of drug and excipients affects these properties and can preclude successful HME-FDM integration (3).

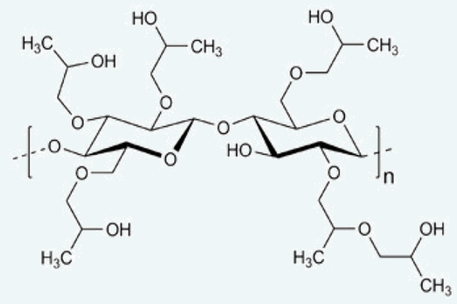
Aim

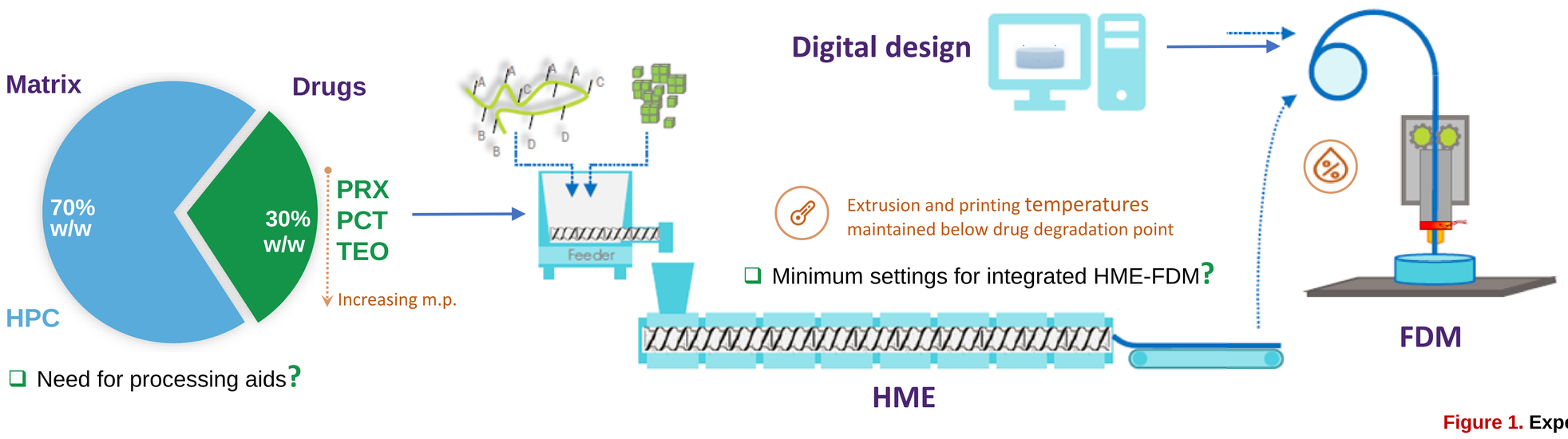
Investigate the impact of the physicochemical properties of drugs and use of excipients on printability and quality attributes of dosage forms

Materials & Methods



Hydroxypropylcellulose
HPC





- Need for processing aids?

Extrudability & printability evaluation

- adequate dimensions & rheology of drug-loaded filaments?
- tablets with simple/complex geometry produced ? meeting Eur. Pharm. requirements for mass and content uniformity?

Figure 1. Experimental set-up and research questions (?)

Results

- Over-plasticization, by water, of HME filaments exposed to ambient relative humidity, affected rheological properties and prevented subsequent printing.
- For printability, each formulation required the addition of plasticizers to lower the melting temperature (e.g. Soluplus, 7.5-15% or trietylcitrate, 5%) and lubricants (e.g. magnesium stearate, 1-3%) to achieve adequate feeding of the filaments to the printer.

Table 1. Characteristics of the model drugs and minimum processing conditions required for integrated HME-FDM

Drug	MW (Da)	Melting point (°C)	Water solubility at 25°C (mg/mL)	HME Temp. (°C)	FDM Temp. (°C)
PRX	374.84	120-138	1.13	120	200
PCT	151.16	168-172	14.00	100	180
TEO	180.17	270-274	7.36	130	220

Figure 2. Typical FDM 3D-printed tablets with simple and complex geometries

- Although TEO (highest m.p.) required more drastic conditions, PRX (lowest m.p.) was more demanding than PCT (medium m.p.). The temperature ranking followed a similar pattern for HME and FDM (**Table 1**).
- Tablets (**Fig. 2**) were uniform in mass and content; the double extrusion resulted in amorphization of every drug tested (PAR exemplified in **Fig. 3**).
- The addition of excipients in the fraction range considered did not impact the temperature required for HME-FDM.

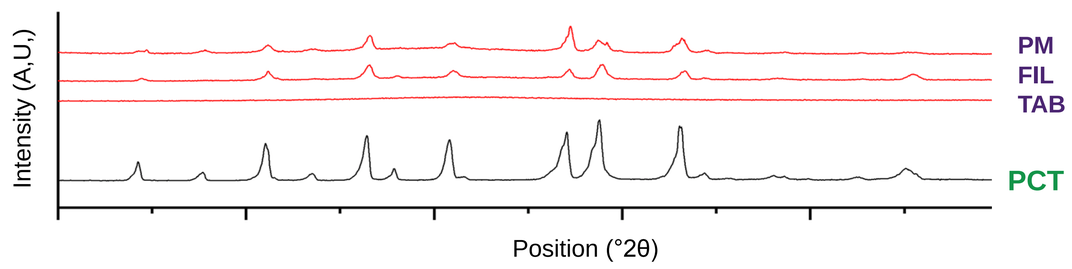


Figure 3. XRD Diffractograms from physical powder mixtures (PM), filaments (FIL) and 3D-printed PCT tablets (TAB) compared to the raw material (PCT)

References

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Acknowledgements

Research funded by Fundação para a Ciência e a Tecnologia, grant number PTDC/CTM CTM/30949/2017 (Lisboa 010145 Feder 030949) and SFRH/BD/146968/2019

Conclusions

- The work failed to establish a direct relationship between drug melting point and the temperature required for filament production and printing;
- Other factors, such as drug load, solubility, hydrophilicity, or ability to establish drug/matrix molecular interactions affect processability;
- The double application of heat resulted in solid-state interactions and amorphization of drugs;
- It appears that processing settings need to be adjusted on a case-by-case basis but further studies with other drugs are required to substantiate these findings.